

100725-38/ Kreisler 1109-KGB  
022698us/JH/ml

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

APPLICANTS : JOST SEIBLER ET AL.  
SERIAL NO. : 10/658,837  
FILED : October 22, 2002  
FOR : SiRNA MEDIATED GENE SILENCING IN TRANSGENIC ANIMALS  
ART UNIT : To be Assigned  
EXAMINER : To be Assigned

---

Hon. Commissioner of Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**INFORMATION DISCLOSURE STATEMENT**

SIR:

Pursuant to 37 CFR §§ 1.56, 1.97 and 1.98, Applicants respectfully request that the Examiner consider the references listed on the attached Form PTO-1449.

**I. Timeliness, Fees and Certifications in lieu of Fees**

This information disclosure statement is being filed within three months of the filing date of the application, or within three months of entry into the national stage, or before the mailing of a first Office Action on the merits. Pursuant to 37 CFR § 1.97(b), consideration of this information disclosure statement does not require a fee or a statement under 37 CFR § 1.97(e). However, should the Assistant Commissioner determine that a fee is, in fact, due, the Assistant Commissioner is hereby authorized to charge the fee to Deposit Account No. 14-1263.

Application No. 10/685,837  
Applicants: Jost Seibler  
Information Disclosure Statement

## **II. Copies of Listed References**

Copies of all references listed on the attached Form PTO-1449 are being supplied.

## **III. Concise Statement of Relevance**

All references listed on the attached Form PTO-1449 are in the English language, and, therefore, a concise statement of relevance is not required.

Some of the references listed on the attached Form PTO-1449 are referred to in the specification, which indicates the degree of relevance


Some of the references listed on the attached Form PTO-1449 were cited in the partial search report issued by the European Patent Office and/or the International search report, and an English-language version of the search reports, which indicates the degree of relevance found by that Patent Office, are attached.

Application No. 10/685,837  
Applicants: Jost Seibler  
Information Disclosure Statement

Consideration of the foregoing in relation to this application is respectfully requested.

Respectfully submitted,

NORRIS McLAUGHLIN & MARCUS, P.A.

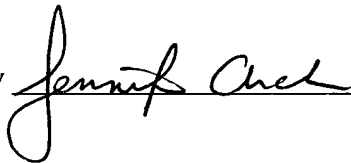
By   
David D. Kim  
Reg. No. 53,123

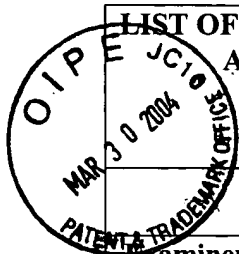
220 East 42<sup>nd</sup> Street  
30<sup>th</sup> Floor  
New York, New York 10017  
(212) 808-0700

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Services as first class mail in an envelope addressed to: Hon. Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on March 25, 2004.

NORRIS McLAUGHLIN & MARCUS, P.A.

By 



<b>LIST OF PATENTS AND PUBLICATIONS</b> <b>APPLICANT'S INFORMATION</b> <b>DISCLOSURE STATEMENT</b> (Form PTO-1449)	Attorney Docket: 100725-38/ Kreisler 1109-KGB	Serial No.: 10//685,837
	Applicant: Jost Seibler et al.	
	Filing Date: October 22, 2002	Group: To Be Assigned

### U.S. PATENT DOCUMENTS

Examiner's Initial		Document Number	Date	Name	Class	Sub Class	Filing Date If appropriate
	AA	5 972 650	26 Oct 1999	Feng Yao	435	69.1	
	AB						
	AC						

### FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Sub Class	Translation Yes No
	AD	02 072762 A ✓	19 Sep 2002	World			
	AE	02 44321 A ✓	6 Jun 2002	World			
	AF						

### OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)

	AG	EPO Search Report, dated 18 December 2002, for EP 02 02 3283. ✓
	AH	Devroe E. and Pamela A. Silver. Retrovirus-delivered siRNA. BMC Biotechnology (2002), 2: 15. ✓
	AI	Brummelkamp, Thijn R, et al. "A system for stable expression of short interfering RNAs in mammalian cells." Science, Vol. 296, No. 5567 (2002) pages 550-553. ✓
	AJ	Paddison, Patrick J et al. "Short hairpin RNAs (shRNAs) induce sequence-specific silencing in mammalian cells." Genes and Development, Vol. 16, No. 8 (2002), pages 948-958 ✓
	AK	Kennerdell, JR and RW Carthew. "Heritable gene silencing using double-stranded RNA." Nature Biotechnology, Vol. 18, No. 8 (2002), pages 896-898. ✓
	AL	Lam, G et al. "Inducible expression of double-stranded RNA directs specific genetic interference in <i>Drosophila</i> ." Current Biology, Vol. 10 (August 2000), pages 957-963. ✓
	AM	Jacque, Jean-Marc et al. "Modulation of HIV-1 replication by RNA interference." Nature, Vol. 418, No. 6896 (2002), pages 435-438. ✓
	AN	Ohkawa, J. et al. "Control of the functional activity of an antisense RNA by a tetracycline-responsive derivative of the human U6 snRNA promoter." Human Gene Therapy, Vol. 11, No. 4 (March 2000), pages 577-585. ✓

**EXAMINER:****DATE CONSIDERED:**

- **EXAMINER:** Initial if Reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformation and not considered, include copy of this form with next communication to applicant.

<b>LIST OF PATENTS AND PUBLICATIONS</b> <b>APPLICANT'S INFORMATION</b> <b>DISCLOSURE STATEMENT</b> (Form PTO-1449)				Attorney Docket: 100725-38/ Kreisler 1109-KGB		Serial No.: 10//685,837	
				Applicant: Jost Seibler et al.			
				Filing Date: October 22, 2002		Group: To Be Assigned	
<b>U.S. PATENT DOCUMENTS</b>							
<b>Examiner's Initial</b>		<b>Document Number</b>	<b>Date</b>	<b>Name</b>	<b>Class</b>	<b>Sub Class</b>	<b>Filing Date If appropriate</b>
	AO						
<b>FOREIGN PATENT DOCUMENTS</b>							
		<b>Document Number</b>	<b>Date</b>	<b>Country</b>	<b>Class</b>	<b>Sub Class</b>	<b>Translation Yes      No</b>
	AP						
<b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>							
	AQ	Yu, Jenn-yah et al. "RNA interference by expression of short-interfering RNAs and hairpin RNAs in mammalian cells." Proceedings of the National Academy of Sciences of USA, National Academy of Sciences, Vol. 99, No. 9 (April 30, 1999), pages 6047-6052. ✓					
	AR	Elbashir, Sayda M. et al. "Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells." Nature, Vol. 411, No. 6836 (May 24, 2001), pages 494-498. ✓					
	AS	Fire, A. et al., Potent and specific genetic interference by double stranded RNA in <i>Caenorhabditis elegans</i> , Nature, Vol. 391, Pages 806-811 (1998). ✓					
	AT	McCaffrey, A.P. et al., RNA interference in adult mice, Nature, Vol. 418, Pages 38-39 (2002). ✓					
	AU	Lewis, D.H. et al., Efficient Delivery of siRNA for inhibition of gene expression in postnatal mice, Nature Genetics, Vol. 32, Pages 107-108 (2002). ✓					
	AV	Paul, C.P. et al., Effective expression of small interfering RNA in human cells, Nature Biotechnology, Vol. 20, Pages 505-508 (2002). ✓					
	AW	Kovalenko et al., The tumor suppression CYLD negatively regulates NF-κB signaling by deubiquitination. Nature, Vol. 424, Pages 801-805 (2003). ✓					
	AX	Brummelkamp, Thijn et al., Loss of the cylindromatosis tumour suppressor inhibits apoptosis by activating NF-κB. Nature, Vol. 424, Pages 797-801 (2003). ✓					
	AY	Carmell, Michelle A. et al., Germline transmission of RNAi in mice, Nat. Struct. Biol., Vol. 10, No. 2, Pages 91-92 (2003). ✓					
	AZ	Gossen, Manfred and Hermann Bujard, Tight control of gene expression in mammalian cells by tetracycline-responsive promoters. Proc. Natl. Acad. Sci. USA, Vol. 89, Pages 5547-5551 (1992). ✓					
<b>EXAMINER:</b>					<b>DATE CONSIDERED:</b>		
• <b>EXAMINER:</b> Initial if Reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformation and not considered, include copy of this form with next communication to applicant.							

<b>LIST OF PATENTS AND PUBLICATIONS</b> <b>APPLICANT'S INFORMATION</b> <b>DISCLOSURE STATEMENT</b> (Form PTO-1449)				Attorney Docket: 100725-38/ Kreisler 1109-KGB		Serial No.: 10//685,837	
				Applicant: Jost Seibler et al.			
				Filing Date: October 22, 2002		Group: To Be Assigned	
<b>U.S. PATENT DOCUMENTS</b>							
<b>Examiner's Initial</b>		<b>Document Number</b>	<b>Date</b>	<b>Name</b>	<b>Class</b>	<b>Sub Class</b>	<b>Filing Date</b> If appropriate
	BA						
<b>FOREIGN PATENT DOCUMENTS</b>							
		<b>Document Number</b>	<b>Date</b>	<b>Country</b>	<b>Class</b>	<b>Sub Class</b>	<b>Translation</b> Yes No
	BB						
<b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>							
	BC	Hermann, Michael T. et al. An epi-allelic series of p53 hypomorphs created by stable RNAi produces distinct tumor phenotypes in vivo. <i>Nature Genetics</i> , Vol. 33, No. 3, Pages 396-400 (2003).					
	BD	Hasuwa, H. et al. Small interfering RNA and gene silencing in transgenic mice and rats. <i>FEBS Letters</i> , Vol. 532, Nos. 1-2, Pages 227-230 (2002).					
	BE	Kovalenko, Andrew et al., The tumour suppressor CYLD negatively regulates NF-kB signaling by deubiquitination, <i>Nature</i> , Vol. 424, Pages 801-805 (2003).					
	BF	Kunath, Tilo et al., Transgenic RNA interference in ES cell-derived embryos recapitulates a genetic null phenotype. <i>Nature Biotechnology</i> , Vol. 21, Pages 559-561 (2003).					
	BG	Rubinson, Douglas A. et al. A lentivirus-based system to functionally silence genes in primary mammalian cells, stem cells and transgenic mice by RNA interference. <i>Nature Genetics</i> . Vol. 33, No. 3, Pages 401-406 (2003).					
	BH	Sui, Guangchao et al. A DNA vector-based RNAi technology to suppress gene expression in mammalian cells. <i>Proc. Nat'l Acad. Sci. USA</i> . Vol. 99, Pages 5515-5520 (2002).					
	BI	Xia, H. et al., siRNA-mediated gene silencing in vitro and in vivo. <i>Nature Biotechnology</i> , Vol. 10, Pages 1006-10 (2002).					
	BJ	Friedrich, Glenn and Philippe Soriano. Promoter traps in embryonic stem cells: a genetic screen to identify and mutate developmental genes in mice. <i>Genes Dev.</i> , Vol. 9, Pages 1513-23 (1991).					
	BK	Hogan, B. et al. Isolation, Culture and Manipulation of Embryonic Stem Cells. <i>Laboratory Manual. In Manipulating the Mouse Embryo</i> , Cold Spring Harbor Laboratory Press, Pages 253-289.					
	BL						
	BM						
<b>EXAMINER:</b>				<b>DATE CONSIDERED:</b>			
• <b>EXAMINER:</b> Initial if Reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered, include copy of this form with next communication to applicant.							